REMARK

Support for amended claims

Support for the amended claims can be found in claims 10-45 as originally filed and as correctly renumbered by the Office in the Official Action of May 21, 2003. Claim 80 is supported by the 6,335,201 patent (ser. no. 09/358,504), which was incorporated into the present application by reference. No new matter has been added.

Case synopsis

The challenge to examine signaling networks and other intricate webs of cellular activity, requires devising powerful techniques that permit not only analyzing these complex interactions, but also enables accurate interpretation of the resulting data. Studying one molecule at a time (the classic "reductionist" approach), has been a powerful tool, but does not efficiently unravel complex signaling pathways. The presently claimed invention meets this challenge.

The claimed invention provides methods that permit simultaneous analysis of the activities of a plurality of different proteins. As needed, the scientist can also compile the activities of multiple proteins, under a barrage of conditions, from which maps of cellular activity may be drawn.

The presently claimed methods measure the activities of a plurality of different proteins (the "targets") by introducing one or more reporter molecules into the target cell. The reporter molecules are sensitive to the activities of the target proteins. After releasing the reporter molecules--altered, unaltered, or both--, the reporter molecules are detected. The activities of the target proteins are determined either by (1) measuring the remaining unmodified reporter molecules (an indirect measure of reporter modification); (2) measuring the produced altered reporter molecules, or (3) comparing unaltered reporter molecules to altered reporter molecules. By performing a series of experiments at different time points and under varying conditions, databases can be developed into valuable repositories that allow for meaningful analysis of the activities of multiple proteins, permitting the untangling of complicated signaling webs, and for understanding the molecular mechanisms of cell behavior.

35 USC §103(a)

The rejection of the claims under 35 USC §103(a) over Day *et al.* (Day et al., 1998) taken with Sims *et al.* (Sims and Allbritton, 1998) in view of Magal (Magal, 1999) and Wright (Wright Jr, 1997) is respectfully traversed. The references fail to teach detecting the activities of a plurality of different proteins with reporter molecules.

Because the presently filed application is entitled to the priority date of March 6, 1998, Day *et al.* (1998) reference is unavailable as prior art under 35 USC §103(a) because it was not published until November, 1998. Please see discussion below, "*Rejection of the claim for priority under 35 USC §119(e).*"

However, even if Day *et al.* (1998) were available as prior art, the invention is still non-obvious. Day *et al.* (1998) introduced a luciferase green fluorescent chimeric protein (that is, a single protein) into cells, using the green fluorescent protein to detect those cells that also express luciferase at high levels for single-cell transcription activity assays (page 848, column 3, lines 10-31). Sims *et al.* (1998) teach the injection of labeled inositol phosphates into cells to ascertain the rate of inositol triphosphate metabolism and detection using high-performance liquid chromatography (HPLC; Abstract and page 4053, *Methods*); Sims *et al.* do *not* suggest detecting and quantifying multiple different proteins (page 4052, column 2, lines 1-25). Magal (1999) teaches the administration of glial cell line-derived neurotrophic factor (GDNF; that is, a single protein) to the middle ear through mini-pumps and vinyl tubing, (column 30, line 46 to column 31, line 23 and column 33, line 29 to column 34, line 27). Wright (1997) teaches the *separation* and *purification* of antigens specific for benign prostate hyperplasia (BPH) to make antibodies (column 16, line 64 to column 17, line 6).

The presently claimed invention is directed to detecting activities of a plurality of different protein with reporter molecules. The references do not alone or combined teach *detecting* a *plurality* of protein activities using reporter molecules. The rejection is respectfully requested to be withdrawn.

35 USC §112, 2nd paragraph

The rejections of the claims under 35 USC §112, 2nd paragraph have been obviated by amendment. Applicants thank the Office for pointing out these formal matters involving the claims.

Rejection of the claim for priority under 35 USC §119(e)

The denial for priority under 35 USC §119(e) is respectfully traversed. The entitlement to priority is determined on a claim-by-claim basis. The Office has made a sweeping denial of priority without providing such an analysis.

When a claim of priority under 35 USC §119(e) is asserted, the claimed *provisional* application is relevant. Support in application 60/252,861 for "detecting activity" can be found, for example, on page 9, lines 10-14 and pages 25-26; microinjection is supported, for example, on page 13, lines 5-6 and 10-11 and in Figure 8. When a claim of priority is asserted to a non-provisional application, 35 USC §120 applies, for which the applicants are also entitled. For example, application 09/036,706 supports detecting activities of a plurality of proteins (column 9, lines 24-31 and column 11, lines 7-64).

The denial is respectfully requested to be withdrawn.

Applicants submit that the application is in condition for allowance. Early notice of such action is respectfully requested.

Cited references

Day, R.N., M. Kawecki, and D. Berry. 1998. Dual-function reporter protein for analysis of gene expression in living cells. *Biotechniques*. 25:848-50, 852-4, 856.

Magal, E. 1999. Method for preventing and treating sensorineural hearing loss and vestibular disorders using glial cell line-derived neurotrophic factor (GNDF) protein product/ US Patent 5,929,041.

Sims, C.E., and N.L. Allbritton. 1998. Metabolism of inositol 1,4,5-trisphosphate and inositol 1,3,4,5-tetrakisphosphate by the oocytes of Xenopus laevis. *J Biol Chem*. 273:4052-8.

Wright Jr, G. 1997. Antibodies reactive with biological markers of benign prostate hyperplasia/ US Patent 5,639,656.

Respectfully submitted,

SONNENSCHEIN NATH & ROSENTHAL LLP
P.O. Box #061080
Wacker Drive Station
Sears Tower
Chicago, Illinois 60606-1080

Gregory M. Zinkl, Ph.D.
Registration No. 48,492
Phone (312) 876-8936